High Thoracic Epidural Anesthesia in Coronary Artery Bypass Surgery: A Propensity-Matched Study

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Objectives: **To assess if 2 different anesthesia strategies, high-thoracic epidural anesthesia (HTEA) plus inhalation anesthesia and total intravenous anesthesia (TIVA) with sufentanil/propofol had different influence on outcomes of coronary artery bypass graft (CABG) surgery patients.**

Design: **Retrospective comparison of outcomes between HTEA and TIVA patients using propensity score pair-wise matching of patients.**

Setting: **A university teaching hospital.**

Participants: **A study of 1,473 consecutive patients undergoing elective CABG surgery; of these, 476 (32%) received HTEA combined with inhalation anesthesia, whereas 997 (68%) underwent TIVA alone.**

Interventions: **The patients undergoing CABG surgery were offered the epidural-inhalation anesthetic approach.**

Measurements and Main Results: **Propensity matching yielded 389 pairs of patients. Patients were well matched in preoperative and operative features. Postoperative mortality, myocardial infarction, stroke, acute renal failure rates, and intensive care unit (ICU) stay were not statistically different in HTEA and TIVA groups. On the other hand, patients treated with HTEA had shorter ventilation times (5.8 ± 3.11 *v* 6.9 ± 5.0 hours, HTEA and TIVA, respectively, $p < 0.001$); in addition, vasoconstrictors were more frequently used in cases of HTEA, whereas vasodilators were mainly used with TIVA both intra- and postoperatively. No neurologic complications related to the use of HTEA were observed.**

Conclusions: **HTEA and TIVA provided similar early outcomes after CABG surgery, and there were no major differences between these 2 strategies in the average risk CABG patient populations. Although HTEA did not cause neurologic problems and yielded a significant reduction in time to extubation, a consistent benefit over standard techniques could not be shown.**

KEY WORDS: anesthesia, epidural, coronary artery bypass, anesthetics, inhalation, outcome

HIGH THORACIC epidural anesthesia (HTEA), administered in addition to general anesthesia, has been extensively investigated because of its potential beneficial effects including perioperative stress response attenuation,[1,2] cardiac sympathetic nerve blockade, and excellent analgesia.[3] Moreover, HTEA dilates epicardial coronary arteries,[4,5] partly normalizes the myocardial blood flow in response to sympathetic stimuli,[6] improves left ventricular function,[7-9] has anti-ischemic properties,[10] and reduces postoperative release of cardiac troponin I (cTnI)[9] and T (cTnT).[2] Unfortunately, these beneficial effects are only potential; in fact, they have not improved clinical outcomes in patients receiving this additional anesthetic technique. The use of HTEA in patients who receive perioperative anticoagulation has been questioned because of the theoretical increased risk of epidural hematoma formation facilitated by full anticoagulation.[11,12] Evidence from randomized trials has not been conclusive.[1,2,9,13-21] Furthermore, the fact that the occurrence of major postoperative complications is usually low, in the range of 1% to 5%, strongly limits the power of these studies to detect significant differences.

The aim of the present study was to compare the incidence of perioperative complications occurring after coronary artery bypass graft (CABG) procedures in 2 groups of patients receiving different anesthetic regimens: HTEA supplemented by sevoflurane or total intravenous anesthesia (TIVA) with sufentanil and propofol. Propensity-modeling techniques[22] were used with a large database of isolated consecutive patients who underwent on- or off-pump CABG surgery at a single institution.

METHODS

After institutional review board approval, an analysis of prospectively collected data entered into the computerized database identified 1,473 patients along with their preoperative, intraoperative, and postoperative variables who underwent elective, full sternotomy CABG surgery from January 2002 to October 2004. The institutional review board waived the requirement for individual patient consent for this retrospective study. Patients were eligible for HTEA after signing informed consent and after fulfilling the following inclusion criteria: (1) stable angina with a documented stenosis diameter of at least 50% in 2 or more epicardial coronary arteries, (2) prothrombin time >80% and partial thromboplastin time in the normal range, (3) platelet counts >100,000/mL), (4) left ventricular ejection fraction >30%, and (5) age >18 years. Exclusion criteria were (1) emergent or urgent operation, (2) known coagulative disorders or recent thrombolytic therapy, (3) angina on arrival in the operating room, (4) acute myocardial infarction in the previous 7 days, (5) clinically significant associated valvular disease, (6) known neuraxial pathology, and (7) patients participating in other clinical research protocols. Anticoagulant and antiplatelet drug policy was the following: patients on oral anticoagulants were excluded from the HTEA procedure unless the therapy had been stopped at least 4 days before surgery and the PT value was in the normal range; and low doses of low–molecular-weight heparin (4,000 U/d) had to be stopped 12 hours before HTEA, whereas higher low–molecular-weight heparin doses (4,000 U twice daily or 8,000 U) had to be discontinued for a minimum of 24 hours before surgery. Also, subcutaneous or intravenous heparin was stopped, respectively, 4 and 6 hours before the procedure; whereas antiplatelet drugs were continued until the morning of surgery with the exception of ticlopidine, clopidogrel, and GP IIb/IIIa inhibitors that were stopped, respectively, 2 weeks, 1 week, and 2 days before surgery. All routine cardiac medications were continued until the morning of surgery.

Premedication consisted of morphine, 0.1 mg/kg, and atropine, 0.07 mg/kg, intramuscularly, 1 hour before surgery; and intravenous (IV) cefazoline, 30 mg/kg, was injected before instrumentation. Monitoring included 5-channel ECG with continuous ST-segment analysis (leads II

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and V5), radial artery catheter, pulse oximetry, and triple-lumen catheter (Multi-Med M3720HS; Baxter, Irvine, CA) or a pulmonary artery catheter (Swan Ganz 13HF7; Edwards Lifesciences, Irvine, CA) inserted through the right internal jugular vein. Transesophageal echocardiography was used following institutional protocols. The HTEA technique has been previously described[23] and is summarized here. With the patient in the sitting position on the operating room table, a 19-G flexible-tip polyurethane catheter (FlexTip Plus; Arrow, Reading, PA) was inserted and advanced 4 to 5 cm cephalad in the epidural space through a 17-G Tuohy needle at the Th1-Th2 or Th2-Th3 interspace using the median approach and the hanging-drop or the loss-of-resistance technique. After aspiration for blood or cerebrospinal fluid, a 2-mL test dose of 2% lidocaine was injected to rule out subarachnoid placement of the catheter. The patients were placed in the supine position, and the time point of epidural puncture was recorded. HTEA was induced by epidural administration of 0.1 mL/kg of a mixture of 0.5% ropivacaine and sufentanil, 2.5 μg/mL, as a loading dose. After 15 minutes, the loss of sensation to cold and to pinprick was tested, and the upper and lower levels were recorded. The induction of general anesthesia was then achieved with fentanyl, 2 to 3 μg/kg, plus thiopental, 3 to 6 mg/kg; pancuronium, 0.1 mg/kg, facilitated tracheal intubation, and the lungs were ventilated at normocapnia with sevoflurane (Sevorane, Abbott) in an air-oxygen mixture. Anesthesia was maintained by a continuous epidural infusion of 0.2% ropivacaine and sufentanil, 1 μg/mL, (0.1 mL/kg/h) and inhalation of sevoflurane. Additional bolus doses of pancuronium were injected if necessary.

The TIVA technique consisted of sufentanil, 0.3 μg/kg, and thiopental, 3 mg/kg, as induction drugs followed by sufentanil boluses of 50 to 100 μg (up to 5 μg/kg), continuous propofol infusion (3 mg/kg/h), and pancuronium, 0.1 mg/kg, for muscle relaxation. After tracheal intubation, the patients were ventilated at normocapnea in an air-oxygen mixture. Additional boluses of pancuronium were injected when necessary.

After internal mammary artery harvesting, 300 IU/kg of bovine lung heparin was given and anticoagulation was assessed every 30 minutes with a celite-activated coagulation time, with a trigger level for additional heparin set at 440 seconds both in conventional and in OPCAB surgery. The heparin dose was administered after 60 minutes elapsed from epidural puncture. On completion of distal and proximal coronary anastomoses, heparin was antagonized with protamine sulfate at a 1:1 ratio (3 mg/kg). The use of vasoconstrictors, vasodilators, inotropes, or β-blocking agents during surgery followed institutional protocols. A nonpulsatile centrifugal or roller pump, tepid hypothermia (32°-34°C), and hemodilution with a hollow-fiber oxygenator were used in all cases of CABG surgery. Cardiopulmonary bypass flow was kept at 2.4 L/min/m^2 and hematocrit at 18% to 25%. Myocardial protection was achieved by the administration of cold (4°C) antegrade and retrograde multidose blood cardioplegia. All OPCABs were performed via a midline sternotomy; mechanical stability of the coronary arteriotomy area was achieved with a suction stabilizer, and a soft plastic coronary flow shunt was always introduced into the coronary arteriotomy. A heating mattress was used, and infusion of warm fluids was performed to maintain normothermia in the patients operated on without cardiopulmonary bypass (OPCAB). At the end of the procedure, the patients were transferred to the ICU without reversal of muscle relaxant drugs. The patients were ventilated in mandatory minute ventilation mode (Dräger Evita 4, Drager, Germany) and extubated when they fulfilled the following criteria: responding adequately to verbal stimuli, body temperature >36°C, blood loss <100 mL/h, hemodynamically stable with little inotropic support, respiratory rate between 10 to 15 breaths/min, pCO_2 <45 mmHg, and arterial oxygen saturation >93% at an F_IO_2 <50%. Intra- and postoperative hemodynamic management aimed to maintain a mean arterial pressure and a heart rate close to 70 mmHg and 80 beats/min, respectively. Treatment of hypotension required IV fluids until the central venous pressure reached 10 mmHg and subsequent norepinephrine infusion; dobutamine was used when hypokinesis was evident on TEE or cardiac index was <2.2 L/min/m^2. Hypertension was treated with nitroglycerin by infusion.

Postoperative analgesia in HTEA patients was performed by the epidural infusion of a mixture of 0.1% ropivacaine and sufentanil, 1 μg/mL, at a rate of 4 to 10 mL/h supplemented by IV ketorolac, 30 mg, at 8-hour intervals; whereas TIVA patients received IV morphine, 0.05 mg/kg, and ketorolac, 30 mg, at 8-hour intervals. Epidural infusion was maintained generally until the third postoperative day, and the catheters were removed on the surgical ward by an anesthesiologist after checking the coagulation status and the scheduled antiplatelet or anticoagulant therapy.

Patients were identified from the prospective computerized database of the hospital and perioperative variables were retrieved from this database (Appendix 1). To reduce the influence of selection on the comparison of outcomes, the authors used propensity-score pair-wise matching of patients undergoing HTEA to the pool of available patients who underwent TIVA. To do this, logistic regression was used to develop a propensity score for assignment to the HTEA group for all patients who underwent elective CABG surgery.[22] The propensity score was constructed using all the preoperative variables listed in Appendix 1. For this, matching to 5 decimal points was initially performed, followed by 4, 3, 2, and 1 decimal point matching. HTEA patients whose propensity scores deviated more than 0.10 from those of TIVA patients were considered unmatched. This yielded 389 HTEA patients propensity matched to 389 TIVA patients. Descriptive statistics are summarized as mean ± standard deviation or median (interquartile ranges) for continuous variables when indicated, whereas categoric variables are expressed in percentages. Preoperative, intraoperative, and postoperative variables have been compared with analysis of variance, Mann-Whitney, chi-square, and Fisher exact tests when indicated. A p value ≤0.05 was considered significant.

RESULTS

During the study period, HTEA was attempted in 476 patients and successfully performed in 414 patients (87%). Failures (n = 62) were mainly because of the impossibility to find the epidural space (n = 34), occurrence of vagal symptoms (n = 12), epidural catheter positioning failure (n = 6), puncture of the dura (n = 5), inefficacy of analgesia and sympathetic block (n = 2), or a bloody tap (n = 3). No neurologic complications related to the use of HTEA were observed. Twelve of 476 patients experienced vagal symptoms like dizziness, perspiration, pallor, bradycardia, and, later, if not adequately treated, hypotension during or, more often, before HTEA instrumentation when they were positioned in the sitting position. In most cases, returning to the supine position ended this syndrome, whereas in a few cases atropine injection resulted in HR normalization. No patients experienced angina or ST-segment alterations during these episodes. Patients with failed HTEA were excluded from pair-wise matching, whereas the 3 patients experiencing a traumatic tap were observed closely in the ICU for occurrence of neurologic symptoms, and surgery was delayed for 24 hours. Details of HTEA clinical features are reported in Table 1.

Because of the influence of selection, patients undergoing HTEA were younger than TIVA patients (64 ± 10 *v* 66 ± 9 years, $p < 0.001$), had greater preoperative weight (77 ± 11 *v* 76 ± 12 kg, $p = 0.042$), were more likely to be males (90% *v* 81%, $p < 0.001$), were less likely to be diabetics (22% *v* 27%, $p = 0.042$), had a higher preoperative serum creatinine level (1.13 ± 0.45 *v* 1.08 ± 0.26 mg/dL, $p = 0.016$), had a lower

Table 1. HTEA Clinical Features

Successful HTEA (%)	414/476 (86.9%)
Needle insertion at Th1-Th2 intervertebral space level (n)	117
Needle insertion at Th2-Th3 intervertebral space level (n)	297
Time from epidural to heparin administration (min)	91.7 ± 32.7
HTEA induction bolus (mL)	6.89 ± 1.08
HTEA perfusion rate (mL/h)	6.68 ± 1.05

NOTE. Values are mean ± standard deviation or n.

EuroSCORE (3 [1-4] *v* 4 [2-5], $p < 0.001$), were more likely to be reinterventions (4.1% *v* 1.8%, $p = 0.011$), and less likely to have left main disease (12% *v* 18%, $p = 0.03$). Postoperatively, HTEA patients were less likely to be on heparin (28% *v* 41%, $p < 0.001$), nitrates (60% *v* 70%, $p < 0.001$), angiotensin-converting enzyme inhibitors (33% *v* 40%, $p = 0.014$), and more likely to be on calcium channel blockers (36% *v* 30%, $p = 0.024$) (Table 2).

Logistic regression analysis showed that the independent predictors to undergo HTEA were reinterventions ($p < 0.0001$), higher preoperative creatinine levels ($p = 0.0003$), and male sex ($p = 0.028$); whereas TIVA was associated with higher EuroSCORE values ($p < 0.0001$), preoperative heparin therapy ($p = 0.0002$), and preoperative angiotensin-converting enzyme inhibitor therapy ($p = 0.0319$). The C statistic, which is equivalent to the receiver-operating characteristic curve, developed for this model was 0.76.

Preoperative characteristics of HTEA and TIVA propensity-matched patients were well matched (Table 3), including similar extent of coronary artery disease. Hospital death, myocardial infarction, stroke, and renal failure were similar in the HTEA and TIVA patients, as well as ICU stay and the occurrence of perioperative ischemia (Table 4). However, HTEA patients experienced shorter postoperative mechanical ventilation times, and vasoconstrictor/vasodilator drug profiles were significantly different between groups (vasodilators were much more frequent in patients undergoing TIVA both intraoperatively and postoperatively, whereas vasoconstrictors were prevalent in HTEA patients).

Table 2. Comparison of Patient Characteristics in the Entire Patient Population

Variable	TIVA (n = 997)	HTEA (n = 414)	*p* Value
Age (y)	66 ± 9	64 ± 10	<0.001
Weight (kg)	76 ± 12	77 ± 11	0.042
Male sex	811 (81%)	374 (90%)	<0.001
Hypertension	685 (69%)	276 (67%)	0.5
Diabetes	271 (27%)	91 (22%)	0.042
Previous myocardial infarction	482 (48%)	182 (44%)	0.1
Serum creatinine (mg/dL)	1.08 ± 0.26	1.13 ± 0.45	0.016
No. of diseased vessels	3 (2-3)	3 (2-3)	0.8
Left main disease	180 (18%)	48 (12%)	0.003
Previous cardiac operation	18 (1.8%)	17 (4.1%)	0.011
EuroSCORE	4 (2-5)	3 (1-4)	<0.001
Preoperative medications			
β-Blockers	664 (67%)	269 (65%)	0.6
Calcium channel blockers	300 (30%)	150 (36%)	0.024
Converting enzyme inhibitors	397 (40%)	136 (33%)	0.014
Nitrates	699 (70%)	250 (60%)	<0.001
Heparin (IV or subcutaneous)	407 (41%)	116 (28%)	<0.001
Aspirin withdrawal <5 days before surgery	538 (54%)	220 (53%)	0.8

NOTE. Values are n (%), mean ± SD, or median (interquartile range).

Table 3. Comparison of Patient Characteristics in Propensity-Matched Pairs

Variable	TIVA (n = 389)	HTEA (n = 389)	*p* Value
Age (y)	65 ± 9	64 ± 9	0.5
Weight (kg)	77 ± 12	77 ± 12	>0.9
Male sex	353 (91%)	350 (90%)	0.7
Hypertension	265 (68%)	262 (67%)	0.8
Diabetes	98 (25%)	88 (23%)	0.4
Previous MI	165 (42%)	171 (44%)	0.7
Serum creatinine (mg/dL)	1.10 ± 0.24	1.10 ± 0.34	>0.9
No. of diseased vessels	3 (2-3)	3 (2-3)	>0.9
Left main disease	56 (14%)	44 (11%)	0.2
Previous cardiac operation	9 (2.3%)	10 (2.6%)	0.8
EuroSCORE	3 (1-6)	3 (1-5)	0.9
Preoperative medications			
β-Blockers	250 (64%)	252 (65%)	0.9
Calcium channel blockers	130 (33%)	137 (35%)	0.6
Converting enzyme inhibitors	131 (34%)	134 (34%)	0.8
Nitrates	246 (63%)	235 (60%)	0.4
Heparin (IV or subcutaneous)	110 (28%)	113 (29%)	0.8
Aspirin withdrawal <5 days before surgery	217 (56%)	206 (53%)	0.4

NOTE. Values are n (%), mean ± standard deviation, or median (interquartile range).

DISCUSSION

The use of epidural anesthesia and analgesia techniques in patients undergoing cardiac surgery has gained increasing popularity in recent years. In fact, this technique has been considered to be potentially beneficial because it was thought to attenuate the stress response to surgery,[1,2] to reduce the sympathetic tone,[3] and to provide improved postoperative analgesia. These effects should result in improved myocardial perfusion and reduced perioperative myocardial ischemia.[6] Moreover, it was previously shown that HTEA could reduce the risk of postoperative pulmonary complications.[24] Unfortunately, all these potential beneficial effects have not led to improvements of major clinical outcomes of patients. In fact, several randomized studies[9,13,19,20,24] have been unable to report reduced mortality rates in patients undergoing HTEA, probably because of insufficient statistical power. As reported by Liu et al,[25] with low mortality and morbidity rates in patients undergoing CABG surgery, at least 4,600 patients are required in a single randomized controlled trial to detect, with a power of 80%, a reduction in incidences of such events from 2% to 1%. However, even when the results of 15 randomized trials were pooled together in a meta-analysis evaluating a total of 1,178

Table 4. Comparison of Intra- and Postoperative Features in Propensity-Matched Pairs

Variable	TIVA (n = 389)	HTEA (n = 389)	*p* Value
On-pump operation	275 (71%)	292 (75%)	0.2
CPB time (TIVA, n = 275; HTEA, n = 292) (min)	107 ± 30	109 ± 31	0.4
X-clamp time (TIVA, n = 275; HTEA, n = 292) (min)	73 ± 22	75 ± 23	0.2
No. of distal anastomoses	3 (2-4)	3 (2-4)	>0.9
In-hospital mortality	2 (0.5%)	5 (1.3%)	0.5
Perioperative MI	9 (2.3%)	4 (1.0%)	0.2
Acute renal failure	3 (0.8%)	7 (1.8%)	0.2
Atrial fibrillation	31 (8%)	44 (11%)	0.1
CVVH	1 (0.3%)	2 (0.5%)	>0.9
Stroke	2 (0.5%)	4 (1.0%)	0.7
Transitory ischemic attack	1 (0.3%)	1 (0.3%)	>0.9
IABP	0	1 (0.3%)	>0.9
MOF	2 (0.5%)	2 (0.5%)	>0.9
Ventilation time (h)	6.9 ± 5.0	5.8 ± 3.11	<0.001
ICU stay (d)	2.0 ± 1.18	2.0 ± 1.43	0.8
Perioperative ischemia			
Intraoperative, before or during anastomoses completion	35 (9%)	31 (8%)	0.6
Intraoperative, after anastomoses completion	18 (4.6%)	17 (4.4%)	0.9
Postoperative	12 (3.1%)	8 (2.1%)	0.4
Vasodilator drug use			
Intraoperative, before or during anastomoses completion	69 (18%)	29 (7.5%)	<0.001
Intraoperative, after anastomoses completion	58 (15%)	20 (5.1%)	<0.001
Postoperative	149 (38%)	73 (19%)	<0.001
Vasoconstrictor drug use			
Intraoperative, before or during anastomoses completion	7 (1.8%)	202 (52%)	<0.001
Intraoperative, after anastomoses completion	24 (6.2%)	185 (48%)	<0.001
Postoperative	30 (7.7%)	146 (38%)	<0.001
Inotropic drug use			
Intraoperative, before or during anastomoses completion	16 (4.1%)	19 (4.9%)	0.6
Intraoperative, after anastomoses completion	17 (4.4%)	22 (5.7%)	0.4
Postoperative	25 (6.4%)	25 (6.4%)	>0.9

NOTE. Values are n (%), mean ± standard deviation, or median (interquartile range).

Abbreviations: X-clamp time, aortic cross-clamp time; CVVH, continuous venovenous hemofiltration; IABP, intra-aortic balloon pump; MOF, multiorgan failure.

patients, no significant differences in endpoints could be shown.

Similarly, both single randomized studies[13,15,20,24,26,27] and the cited meta-analysis did not show reduced myocardial infarction rates in patients undergoing HTEA. Less information is available concerning other important outcomes. Concerning perioperative renal dysfunction, Scott et al[24] showed that HTEA-treated patients had a significant decrease (from 6.9% to 2%) in the occurrence of this complication, defined as a 2-fold increase of serum creatinine.

One of the potential advantages of HTEA, derived from its physiologic features (coronary vasodilation, myocardial oxygen consumption decrease), is a reduction of myocardial ischemia. Loick et al[2] showed that new ST-segment elevation or depression occurred less frequently in the group of patients treated with HTEA. Accordingly, Berendes et al[9] showed a reduction of regional wall motion abnormalities, detected with transesophageal echocardiography, and a reduction of postoperative ischemia in patients treated with HTEA in comparison to a control group treated with general anesthesia. Nevertheless, the present study could not establish any effect of HTEA on myocardial ischemia based on electrocardiographic changes in this study group. The results are in agreement with the nonstatistically significant decrease of total duration of ischemia shown with Holter monitoring by Priestley et al.[13]

Atrial fibrillation (AF) is one of the most common complications in patients after CABG surgery, and, despite improvements in anesthetics and surgical techniques, it still develops in more than 30% of patients. Increased sympathetic activation contributes to the pathogenesis of AF. Although Scott et al[24] found a statistically significant reduction from 22.3% to 10.2% in the postoperative rate of supraventricular arrhythmias, other authors have not confirmed these positive results.[9,13-17,19,27] It is not clear if the reduction of AF rate could be related to the dose and the concentration of the local anesthetic used in the postoperative course; Jideus et al,[17] Priestley et al,[13] Royse et al,[14] and Nygard et al[19] injected higher local anesthetic doses than Scott et al but did not achieve the same results. The findings of the present study are limited to the duration of ICU stay: AF incidence was not lowered in the group treated with HTEA in comparison with TIVA (11% *v* 8%).

This study is in agreement with many other randomized controlled trials suggesting a reduction in extubation time with use of HTEA. Several authors also previously have reported a statistically significant reduction in time of ventilation.[2,9,13,14,19,20,21,24,26,27] In the present study, ventilation time

decreased from 6.9 ± 5.0 hours (HTEA patients) to 5.8 ± 3.11 (TIVA patients), and no patient of either group needed reintubation. However, the clinical impact of this faster extubation on patient outcomes remains to be shown, and it has been pointed out that similar results may be achieved by other anesthesia techniques.[25]

This study did not focus on pain as an endpoint, but HTEA is superior to any other method of pain control after sternotomy. This previously has been shown by others and confirmed in the meta-analysis by Liu et al.[25] Recently, however, contrasting data were reported[27] showing no differences in visual analog scale (VAS) scores between patient-controlled (PC) TEA and PCA with morphine. However, in their study,[27] VAS scores were reported to be greater than 5 in both groups on the second and third postoperative days (with cough), which is an unacceptable value during postoperative pain therapy. In a previous article,[23] the present authors documented VAS scores for pain during coughing in the first 24-hour period to be <2 in all patients.

In conclusion, the results of this study are consistent with previous studies. No significant differences were detected in HTEA-sevoflurane and TIVA patients in terms of the main outcomes of mortality, myocardial infarction, stroke, and acute renal failure; the need for continuous venovenous hemofiltration, aortic counterpulsation, and multiple-organ failure were remarkably similar in both groups of patients. These results, from a relatively large cohort of propensity-matched patients, confirm and expand the evidence coming from several other previously published studies showing that HTEA-based and opioid-based anesthetic strategies are probably equivalent in terms of endpoints, suggesting that the use of this technique may not improve early outcomes in average risk patients undergoing coronary artery bypass surgery. The potential advantages of HTEA may become evident in high-risk patients, who have higher complication rates, and are the most likely to benefit from a strategy that reduces the stress response to surgical trauma.

APPENDIX: PATIENT VARIABLES CONSIDERED IN ANALYSES

Preoperative data: age (years), weight (kg), sex, hypertension, diabetes, previous myocardial infarction, serum creatinine (mg/dL), number of diseased vessels, left main disease, previous cardiac operation, and EuroSCORE. Medications: use of β-blockers, calcium channel blockers, converting enzyme inhibitors, nitrates, heparin (intravenous or subcutaneous), and aspirin withdrawal <5 days before surgery.

Intra- and postoperative data: on-pump operation, cardiopulmonary bypass time (minutes), cross-clamp time (minutes), number of distal anastomoses, in-hospital mortality, perioperative myocardial infarction, acute renal failure, atrial fibrillation, need for continuous venovenous hemofiltration, stroke, transitory ischemic attack, intra-aortic balloon pump, multiorgan failure, ventilation time (hours), and ICU stay (days).

Perioperative ischemia (intraoperative, before or during anastomoses completion; intraoperative, after anastomoses completion; postoperative).

Vasodilator drug use (intraoperative, before or during anastomoses completion; intraoperative, after anastomoses completion; postoperative).

Vasoconstrictor drug use (intraoperative, before or during anastomoses completion; intraoperative, after anastomoses completion; postoperative).

Inotropic drug use (intraoperative, before or during anastomoses completion; intraoperative, after anastomoses completion; postoperative).

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